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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,352	09/10/2001	Martin John Glenton Hughes	GJE-70	7295

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EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,352	HUGHES ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendment filed on 7/28/03 has been entered into the record. Claims 1-30 have been canceled. New claims 31-42 have been entered. Claims 31-42 are pending in the application.

2. The examiner acknowledges the amendment to the specification, copy of abstract and the specification that contains line numbers and have been placed in the application.

Rejections moot

3. In view of cancellation of prosecuted claims, 1-30, all the rejections of record are moot.

Claim Rejections - 35 U.S. C. § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 31-42 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov). This is a written description rejection.

The specification broadly describes as part of the invention polynucleotide sequences comprising the gene pho3-1, SEQ.ID.NO: 22 encoding the polypeptide, SEQ.ID.NO: 23 from Group B *Streptococcus agalactiae*. However, the specification does not disclose any homologue or functional fragment with 60% or 80% sequence similarity to SEQ.ID.NO: 22 and does not meet the guidelines on written description.

Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the encoding sequence by use of language in which a specified fragment of said polynucleotide sequence or homologs with 60% or 80% sequence similarity to SEQ.ID.NO: 22 that correspond to sequences from other species of Bacteria. However, fragment or homologs with 60% or 80% sequence similarity to SEQ.ID.NO: 22 do not meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequences SEQ.ID.NO: 22 encoding Group B Streptococcus (GBS) M732 the polypeptide of SEQ.ID.NO: 23 from *Streptococcus agalactiae*. The specification fails to teach a single fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22 and a method for treatment or prevention associated with any and all bacterial infections using fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22. The specification fails to teach the structure or relevant identifying characteristics of fragment or homologue with 60% or 80% sequence similarity to SEQ.ID.NO: 22, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed in claims 31-42.

6. Claims 31-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment or prevention of Group B *Streptococcus agalactiae* does not reasonably provide enablement for a method of treating or

preventing all bacterial infections comprising administering to a patient an effective amount of a polypeptide encoded by a functional fragment or homolog, wherein said homologue is obtainable from Group B Streptococcus and has at least 60% or 80% sequence similarity to SEQ.ID.NO: 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Scope of enablement requires that the specification teach those in the art how to make and use the invention commensurate with the scope of the claimed invention without undue experimentation and includes an analysis of: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those the art, and (8) the breadth of the claims.

With regard to %identity, the specification is not enabled for a polypeptide encoded by a polynucleotide fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22 because it is unclear to one skilled in the art what sequences are embraced by the claim. If it is unclear to one skilled in the art what sequences are embraced by a claim which is based on a specification to determine percent identity, the specification is non-enabling, since one skilled in the art would not be able to make and use those sequences without undue experimentation.

Applicant has not set forth which amino acid (s) in a polypeptide encoded by a polynucleotide SEQ.ID.NO: 22 can be deleted or inserted or substituted to give rise to a polypeptide encoded by a polynucleotide fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22. After these alterations or modifications whether a polypeptide encoded by a polynucleotide fragment or homolog with 60% or 80% sequence similarity to

SEQ.ID.NO: 22 can still retain the therapeutic activity in either preventing or treating bacterial infections including *Streptococcus agalactiae* is not set forth in the specification.

The specification provides guidance and direction with regard to a polypeptide encoded by SEQ.ID.NO 22, which is designated as pho 3-1. However, functional fragments or homologs have not been identified. The specification fails to teach a polypeptide encoded by a polynucleotide functional fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22 and it's use in a method for treating bacterial infections. It is well known that for proteins, for example, even a single amino acid change can destroy the function of the biomolecule. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Applicant failed to give direction to what modification have been done to SEQ.ID.NO 22 to give rise to a polypeptide encoded by a polynucleotide fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22 and what changes would have an adverse effect on the function of this peptide is not predictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid

sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 22 can be varied and still achieve a polypeptide functional fragment or homolog with 60% or 80% sequence similarity to SEQ.ID.NO: 22 that is functional in treating bacterial infections. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

Applicants' arguments filed on 7/28/03 have been fully considered with respect to New claims 31-42 but they are not deemed to be persuasive.

Applicant states that homologue is obtainable from GSB that has 60% sequence similarity to SEQ.ID.NO: 22 and brings the examiner's attention to Example 11, page 15 of the specification.

The examiner has reviewed the specification and noted that the homologue to the GBS pho3-1 gene product can be identified in other bacteria such *S.pyogenes, S. pneumoniae, B.subtilis* etc from genome sequence data but annotations to identify gene and gene products

were so far unavailable. Based on the specification, it is clear functional fragments or homologues have not been disclosed.

Applicant further argues that the skilled artisan can determine fragments that retain the immunological properties based on the sequence database search and textbook knowledge. Applicant attached the Hughes et al publication for supporting enablement for the claimed method.

As examiner pointed in the new rejections, theoretical functional fragments or homologues can be prepared using databases etc. However, using such modified fragments, as a therapeutic agent requires undue experimentation on the part of the skilled artisan to practice the invention as claimed as discussed in paragraph # 6.

Status of Claims

7. No claims are allowed.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

10/13/03

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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